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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

09/687,267 10/13/00 GLENN

J 240042052403

| EXAMINER |
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HM12/0214

PENG CHEN  
MORRISON & FOERSTER LLP  
12636 HIGH BLUFF DRIVE  
SUITE 300  
SAN DIEGO CA 92130-2071

| BRUMBACK, B |              |
|-------------|--------------|
| ART UNIT    | PAPER NUMBER |

1642

DATE MAILED:

02/14/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/687,267

Applicant(s)

Glenn

Examiner

Brenda Brumback

Group Art Unit

1642

☐ Responsive to communication(s) filed on \_\_\_\_\_.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 13-21 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 13-21 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 1

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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### **DETAILED ACTION**

1. The preliminary amendment filed 10/13/2000 has been entered as Paper # 2. Claims 1-12 were canceled. New claims 13-21 were added. Claims 13-21 are pending and under examination.

#### ***Information Disclosure Statement***

2. The Information Disclosure Statement filed 10/31/2000 has been considered. A signed copy is attached hereto.

#### ***Specification***

3. The application is objected to because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c). A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

#### ***Claim Objections***

4. Claims 13-21 are objected to because they lack proper introduction. The present Office practice is to insist that each claim be the object of a sentence starting with a phrase such as "I (or we) claim" or "What is claimed is" or "That which is claimed is". See MPEP 608.01 (m). Appropriate correction is required.

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***Claim Rejections - 35 USC § 112***

5. Claims 13-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, and 6) the quantity of experimentation needed.

The instant disclosure fails to enable the invention of claim 13-21 for the following reasons.

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*The nature of the invention:* The instant claims are drawn to a method of treating a viral infection in as subject (*i.e.*, *in vivo* therapy) via inhibiting the prenylation of a protein contained in the virus infecting said subject comprising administering to the subject an agent selected from a peptide that mimics the amino acid sequence of a CXXX, XCXX, XXCX, or XXXC box in the viral protein; an inhibitor of enzymes in the pathway of prenyl lipid synthesis from mevalonate; an inhibitor of a prenyl transferase; and a mimic of a prenyl group.

*The state of the prior art and the predictability or lack thereof in the art:* The art teaches that the efficacy of therapeutics is dependent upon factors such as solubility of the drug, bioavailability at the target site, attainment of effective plasma concentrations, solubility in tissues, biotransformation, toxicity, rate of excretion or clearance, and in the case of antivirals, propensity for emergence of resistant strains (see Benet et al., pp. 3-32, in The Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21. The art further teaches that "the story of drug discovery for viral diseases is replete with failures" (Rice et al., Advances in Pharmacology 33:389-438, 1995; see page 390, first sentence of the third paragraph) and that drugs which are quite effective in the laboratory often reveal disappointing traits in the clinical setting (Rice et al., page 409, last paragraph, second sentence).

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The disclosure teaches that agents which inhibit viral protein prenylation encompass tetrapeptides that are CXXX box analogs (see page 10, last partial paragraph). The art teaches that the effectiveness of agents which inhibit protein prenylation *in vitro* is unpredictable when they are administered *in vivo*. Adequate concentrations of the biologically active inhibitor must be maintained long enough to exert the desired effect on target cells and the agent must be able to penetrate tissues, target the infected cells, and be taken up by the cells. Gibbs (Cell 65:1-4, 1991; of record as reference 11 in the IDS filed 10/31/2000) teaches that "in the case of farnesyl-protein transferase, FPP and tetrapeptides serve as models for inhibitor development. For FPP, the diphosphate prevents cell penetration ... As for tetrapeptides, little is known about their cellular uptake, except that it is very inefficient ... tetrapeptide inhibitors of farnesyl-protein transferase may require significant modification before they are pharmacologically useful" (see the paragraph spanning pages 3-4). Furthermore, the art teaches that protein prenylation inhibitors may result in a nonspecific shutdown of protein prenylation in general (see Hoffman, Science 254:650-651, 1991; page 651, column 1, second and third full paragraphs, of record as reference 17 in the IDS filed 10/31/2000). The art also teaches that inhibitors of viral protein prenylation may be insufficiently soluble for effective *in vivo* use and may be unacceptably toxic and/or carcinogenic (see Rightsel et al., Nature 204:1333-1334, 1964; of record as reference # 33 in the IDS filed 10/31/2000; first full paragraph and the paragraph spanning pages 1333 and 1334) and Detroy et al. (Journal of General Microbiology 92:167-174, 1975, of record as reference # 9 in the IDS filed 10/31/2000, see page 167, abstract and page 168, second full paragraph).

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*The amount of direction or guidance present and the presence or absence of working examples:* In light of the extensive teachings of unpredictability found the art, the specification must contain sufficient guidance as to how to maintain adequate concentrations of biologically active inhibitors *in vivo*, how to target and penetrate virus-infected cells, how to achieve inhibition of viral protein prenylation in the absence of a general shutdown of protein prenylation, and how to achieve a therapeutically effective concentration without significant toxicity. These teachings are absent from the disclosure. There is no guidance provided for overcoming the unpredictability found in the art regarding *in vivo* administration of antiviral therapeutics in general and the claimed agents in particular. There are no working examples describing *in vivo* administration of the claimed agents for treatment of viral infections. In light of the absence of such guidance in the instant specification, it would require undue experimentation by one of skill in the art to practice the claimed invention.

Furthermore, the instant specification fails to enable the embodiment drawn to administration of an mimic of a prenyl group for the following additional reasons. While the disclosure (page 11) and Reiss et al. both teach that mimics of the "CXXX" box inhibit protein prenylation, neither the disclosure nor the art teaches that mimics of prenyl groups inhibit prenylation. The disclosure makes a single statement regarding inhibition by mimics of prenyl groups on page 12, lines 2-3: "Other agents include derivatives and mimics of prenyl groups themselves". The disclosure fails to teach what is encompassed within mimics of the groups. The disclosure fails to provide guidance as to how these mimics can be made or administered. There

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are no teachings that these mimics actually inhibit viral replication either *in vitro* or *in vivo*. There are no working examples describing inhibition of protein prenylation by prenyl group mimics. Absent these teachings, it would require undue experimentation by one of skill in the art to discover these prenyl group mimics and to then determine which, if any, of the mimics would inhibit protein prenylation sufficient to treat a viral infection in a subject.

### *Conclusion*

6. Claims 13-21 are free of the prior art.

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

BB

February 12, 2001

*Brenda Brumback*  
Brenda Brumback,  
Patent Examiner